

REMARKS

The undersigned would like to thank Examiner Raymond for courtesy extended during a personal interview conducted on August 6, 2004.

Claims 1, 3, 4, 6, 8, 9, 11, 13, 14, 16, 28, 29, 31, 43, 44, 46, 48, 49, 51, 53, 54, 56, 58, 59, 61, 68, 69, 71, 78, 79, 81, 83, 84, 86, 88, 89, 91-117, 119-123, 130, 131, 133, 135, 136, 138, 140, 141, 143, 150, 151, 153-159, 161-169 and 171-175 are pending.

The amendments to the claims are supported by the specification at page 2, line 12 to page 5, line 32 and page 6, line 1 to page 9, line 24.

The deletion of page 18, lines 23-32, of the specification has been made to make the disclosure more clear.

The insertion of the X-ray diffraction pattern peaks into the claims should not change the scope of the amended claim recitations because it would have been apparent to one skilled in the art that the various crystalline forms, e.g. B, C, D, F, E1, etc., refer to the crystalline forms as characterized by the X-ray diffraction patterns (XRDs) disclosed in the specification, wherein the XRDs have the peaks recited in the claims.

The other amendments to the claims are cosmetic. For instance, the deletion of "solid" in claim 1 is cosmetic because one skilled in the art would have known that a crystalline form of a compound is a solid. The replacement of "solvate" with "solvent" in claim 1 is also cosmetic because one skilled in the art would have known that a solvated form comprises a solvent. Similarly, the replacement of the hyphenated chemical names with more customary non-hyphenated names in claim 1 is cosmetic and should not change the scope of the amended claim recitations. The replacement of "precipitating" with "isolating" in claims 101, 102, 161 and 162 has been done for grammatical purpose.

Applicants' Statement of Substance of Personal Interview with Examiner

In the personal interview of August 6, 2004, the undersigned indicated that the various forms of lamotrigine claimed in the application would be identified with peaks from the X-ray powder diffraction patterns. In addition, the undersigned argued that the claims were not inherently anticipated by Janes et al since the authors of Janes et al did not use the relevant solvents to crystallize lamotrigine and the lamotrigine crystallized in absolute ethanol was reported to be unstable in X-ray.

Claim Rejections -- 35 U.S.C. 112, 2nd Paragraph

Claims 1-153 were rejected as indefinite for failing to recite the compound, lamotrigine, in its IUPAC name or for referring to a drawing. Applicants respectfully traverse the rejections. The recitations of lamotrigine have been replaced with its chemical name, “6-(2,3-dichlorophenyl)-1,2,4-triazine-3,5-diamine.”

Claim 1 was also rejected as indefinite for lacking the structure of the solvate claimed. Applicants respectfully traverse the rejection because it is clear that the solvate claimed is a substance comprising 6-(2,3-dichlorophenyl)-1,2,4-triazine-3,5-diamine and a solvent as recited in claim 1. One skilled in the art would have understood that the solvate of 6-(2,3-dichlorophenyl)-1,2,4-triazine-3,5-diamine has molecules of the solvent incorporated in the crystalline structure.

Claims that merely recite a crystalline form of 6-(2,3-dichlorophenyl)-1,2,4-triazine-3,5-diamine without any properties recited have been canceled (e.g. claims 2, 7, 12, etc.) Claims that refer to drawings have also been canceled (e.g. claims 5, 10, etc.). Claims that are drawn to the crystalline forms of 6-(2,3-dichlorophenyl)-1,2,4-triazine-3,5-diamine have been amended with the insertion of the peaks from the X-ray powder diffraction patterns that characterize the particular crystalline forms. The insertion of the peaks from the X-ray powder diffraction patterns should not narrow the scope of the amended claim recitation because one skilled in the art would have understood that the crystalline forms recited in the claims refer to the crystalline forms disclosed in the specification with the appropriate X-ray powder diffraction patterns.

Claims 124 and 125 were rejected as contradictory for allegedly reciting different X-ray powder diffraction patterns for the same crystalline form E. Applicants respectfully traverse the rejection because claim 124 recites several peaks of the X-ray powder diffraction pattern that can be used to characterize crystalline form E of 6-(2,3-dichlorophenyl)-1,2,4-triazine-3,5-diamine, and claim 125 recites further peaks of the X-ray powder diffraction pattern that can be used to characterize the same crystalline form E. Applicants submit that claims 124 and 125 are not contradictory.

Withdrawal of the indefiniteness rejections is requested.

Claim Rejection -- 35 U.S.C. 102

Applicants respectfully traverse the anticipatory rejection of claims 1-16, 26-31, 42-61, 67-71, 77-93 and 124-153 over Janes et al., Acta. Cryst., (1989, C45, 129-132) based on inherency.

Applicants have discovered novel crystalline forms of lamotrigine, i.e. 6-(2,3-dichlorophenyl)-1,2,4-triazine-3,5-diamine, and methods for preparing them. The novel crystalline forms are characterized by XRPDs and thermal analysis. Some of the novel crystalline forms of 6-(2,3-dichlorophenyl)-1,2,4-triazine-3,5-diamine are designated as forms B, C, D, E1, F, H, J, K, L, M, N, P, Q, R, S, and U, and listed below for the convenience of Examiner Raymond:

- form B (monosolvate of DMF),
- form C (sesquisolvate of DMF),
- form D (2/3 solvate of DMF),
- form E1 (2/3 ethanolate),
- form F (1/3 acetate),
- form H (monosolvate of ethanol),
- form J (monosolvate of isopropanol),
- form K (monosolvate of THF),
- form L (monosolvate of acetone),
- form M (monosolvate of DMA),
- form N (monohydrate),
- form Q (monosolvate of isopropanol),
- form R (monosolvate of methyl-isobutyl-ketone),
- form S (anhydrous), and
- form U (monosolvate of methyl tertiary-butyl ether).

Janes et al. merely describes (1) a lamotrigine methanol solvate (monoclinic P2₁/n), and (2) a form of lamotrigine having monoclinic space crystallized from absolute ethanol (see the Abstract and page 131, right column, the last two paragraphs). There is simply no disclosure of any solvate of DMF (forms B, C, D), acetone (forms F, L), isopropanol (forms J, Q), THF (form K), DMA (form M), hydrate (form N), or methyl isobutyl ketone (forms R and U). Janes et al is also silent on any anhydrous form of lamotrigine, so Janes et al does not disclose form S. Thus, there could be no inherent disclosure of forms B, C, D, F, J, K, L, M, N, P, Q, R, S and U of lamotrigine now claimed.

Claims 125, 126, 128 and 160 are directed toward a 2/3 methanolate, form E, of lamotrigine. Claims 145, 146, 148 and 170 are directed toward another 2/3 methanolate, form O, of lamotrigine. Applicants submit that Janes et al does not disclose form E or O. To

advance prosecution, however, claims 125, 126, 128, 145, 146, 148, 160 and 170 were canceled.

Claims 130, 131, 133 and 161 are directed toward a 2/3 ethanolate, form E1, of lamotrigine. Claims 135, 136, 138, 163 and 164 are directed toward a monoethanolate, form H, of lamotrigine. These two claimed ethanolates (forms E1 and H) are different from the form of lamotrigine crystallized from absolute ethanol in Janes et al. These two claimed ethanolates are **stable** in X-rays. The present inventors were able to determine the X-ray diffraction patterns of form E1 or H. In contrast, Janes et al discloses that the form of lamotrigine crystallized from absolute ethanol is relatively **unstable** to X-rays (see page 131, right column, the second to the last sentence). Thus, to the extent that Janes et al might disclose an ethanolate of lamotrigine, the ethanolate of Janes et al is different from the ethanolates of claims 130, 131, 133, 161, 135, 136, 138, 163 and 164.

Inherency may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient. *In re Oelrich and Divigard*, 666 F.2d 578 (CCPA 1981). Anticipation by inherency requires that 1) the missing descriptive matter be "necessarily present" in the prior art reference and that 2) it would be so recognized by persons of ordinary skill in the art. *Continental Can Co. v. Monsanto Co.*, 948 F.2d 1264 (Fed.Cir. 1991). When prior art fails to disclose a method for making a claimed compound, at the time the invention was made, it cannot be legally concluded that the compound itself is in the possession of the public. *Ashland Oil, Inc. v Delta Resins & Refractories, Inc.* 776 F.2d 281 (Fed. Cir. 1985).

Some of the instant claims are directed toward methods of preparing crystalline forms of lamotrigine. However, Janes et al is totally silent on any method of preparing any crystalline form of lamotrigine. Janes et al fails to anticipate these method claims.

Withdrawal of the anticipatory rejection is requested.

CONCLUSION

In view of the above reasoning, applicants submit that the application is in a condition for allowance. A Notice of Allowance is believed in order. In the event that there remains any issue that can be resolved with a telephone interview, Examiner Raymond is encouraged to call the undersigned.

If this paper is deemed not timely, applicants petition for an appropriate extension of time. The petition fee, and any other fees that may be required in relation to this paper, can be charged to Deposit Account No. 11-0600, referencing Docket Number 01662/56302.

Respectfully submitted,
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Date: September 29, 2004

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